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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/728,055	12/04/2003	George Mulligan	MPI02-202P1RNM	8930

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MILLENNIUM PHARMACEUTICALS, INC.
40 Landsdowne Street
CAMBRIDGE, MA 02139

EXAMINER	
REDDIG, PETER J	
ART UNIT	**PAPER NUMBER**
1642	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
31 DAYS	01/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/728,055	MULLIGAN ET AL.	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,7,10,25,26 and 29-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,2,4,5,7,10,25,26 and 29-41* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Election filed 10/26/2006 in response to the Office Action of 5/22/2006 is acknowledged and has been entered.

2. Applicants have canceled claims 3, 6, 8, 9, 11-24, and 27-28. Applicants have amended claims 1, 2, 4, 25, and 26 and have added new claims 29-41.

3. Applicant's election with traverse of Group II, claims 1, 2, 4-10, 25, and 26 drawn to the predictive marker Number 149 and the species multiple myeloma is acknowledged.

4. Applicants argue that the Examiner has divided the 28 claims of the present application into 6 main groups, and further divided the claims according to a single marker per group. Applicants argue that this ignores the fact that claims 21 and 22, of Group I recites "at least two" for a marker set. Applicants argue that the examiner appears to be preparing to search the invention in terms of pure molecular sequences. Applicants argue that the consequence of this is that the effective number of groups will number in the thousands, which ignores many of the teachings of the Applicants.

Applicants argue that there is an alternative position from which to view the claims. Applicants request that the Examiner consider that the Restriction be viewed in terms of treatment method in general, rather than getting mired in the details of the individual markers. Applicants argue that, for some time, the prediction of disease by marker analysis has been moving away from analysis of single markers and toward the analysis of multiple markers. Applicants argue that this genetic profiling has become scientifically and commercially accepted (see, e.g., Van de Vijver et al. and Barden et al., provided in the IDS). Applicants argue that the markers provided in Tables 1, 2 and 3 can be viewed as starting material for predictive marker

sets associated with responsiveness, non-responsiveness, time-to-progression, or refractory nature of tumors for which bortezomib treatment is contemplated. Applicants argue that Tables 4-8 represent studies wherein various statistical or scientific methods were applied to provide non- limiting examples where the principles of generating predictive marker sets were applied or validated. Applicants argue that only "bortezomib" needs to be searched in relation to a liquid tumor and genetic profiling or predictive marker sets for the claims of Group II as currently amended. Then, the overall content of Table 1 (e.g., total number of genes, whether the profile or marker set predicts responsiveness, non-responsiveness, time-to-progression, or refractory nature of tumors, the names of probe sets or representative genes, relative rank of markers, etc) can be perused in any resultant profiles or sets identified in the search.

Upon review and reconsideration, and in view of the limitation "at least one" in original claim 4 and "at least two" in original claims 21 and 22, Applicants should not have been limited to choosing a Group with only one predictive marker. However, the argument that Group II could be searched on the basis of bortezomib, liquid tumor, and genetic profiling/predictive markers alone is not found persuasive because this would not take into account all of the limitations of the claims.

A telephone call was made to Tracy Sioussat on December 12, 2006 to request an oral election of a species of one or a specific combination of more than one feature from the Predictive Markers in Table 1, but did not result in an election being made.

The restriction requirement of 5/22/2006 is hereby vacated and the new restriction requirement follows.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

Claims 1 links inventions I and II. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claim 1. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP ' 804.01.

I. Claims 2, 4, 5, 7, 10, and 29-33 drawn to a method for determining a bortezomib therapy regimen for treating a liquid tumor in a patient, wherein the level of the expression of the feature in the predictive marker set is determined by detection of mRNA, classified in class 435, subclass 6.

(Upon election of Group I, applicant must further choose one feature or a specific, defined combination of features from the Predictive Markers in Table 1 as each feature represents an independent invention, not a species)

It is noted for Applicant's convenience that this is a requirement for the election of a Group for examination NOT a requirement for an election of species because although the claims are presented in Markush format, the claims are drawn to methods using multiple agents which do not share, as a whole, a substantial structural feature disclosed as being essential to their utility. Thus, the analysis of the claims, for restriction purposes, is subject to the findings of the court wherein the court found that unity of invention exists where entities included within a Markush group share a substantial structural feature disclosed as being essential to utility of the invention, In re Harnisch, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Since the members of the group do not share a substantial structural feature disclosed as being essential to utility of the invention, the group as claimed fails the Harnisch test and the claims are not accorded Markush

restriction practice because they do not meet the requirements to be accorded Markush practice under MPEP 803.02.

The above inventions are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the patentability of the combination does not rely necessarily and solely on the patentability of any one subcombination and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the patentability of the combination does not rely necessarily and solely on the patentability of any one subcombination as clearly evidenced by the plural subcombinations claimed. Further, each of the subcombinations has utility by itself because each of the subcombinations is useful for screening for different variables and different markers. Thus the claims are distinct as required by MPEP 806.05(c).

II. Claims 4, 5, 7, 10, and 29-33 drawn to a method for determining a bortezomib therapy regimen for treating a liquid tumor in a patient, wherein the level of the expression of the feature in the predictive marker set is determined by detection of protein, classified in class 435, subclass 7.1.

(Upon election of Group II, applicant must further choose one feature or a specific, defined combination of features from the Predictive Markers in Table 1 as each feature represents an independent invention, not a species)

It is noted for Applicant's convenience that this is a requirement for the election of a Group for examination NOT a requirement for an election of species because although the claims are presented in Markush format, the claims are drawn to methods using multiple agents which do not share, as a whole, a substantial structural feature disclosed as being essential to their utility. Thus, the analysis of the claims, for restriction purposes, is subject to the findings of the court wherein the court found that unity of invention exists where entities included within a Markush group share a substantial structural feature disclosed as being essential to utility of the invention, In re Harnisch, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Since the members of the group do not share a substantial structural feature disclosed as being essential to utility of the invention, the group as claimed fails the Harnisch test and the claims are not accorded Markush restriction practice because they do not meet the requirements to be accorded Markush practice under MPEP 803.02.

The above inventions are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the

patentability of the combination does not rely necessarily and solely on the patentability of any one subcombination and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the patentability of the combination does not rely necessarily and solely on the patentability of any one subcombination as clearly evidenced by the plural subcombinations claimed. Further, each of the subcombinations has utility by itself because each of the subcombinations is useful for screening for different variables and different markers. Thus the claims are distinct as required by MPEP 806.05(c).

Claim 25 links inventions III and IV. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claim 25. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP ' 804.01.

III. Claim 26, drawn to a kit for determining a bortezomib therapy for treating a tumor in a patient comprising reagents for assessing the expression of the predictive marker set of claim 1 and instructions for use, drawn to detecting nucleic acids, classified in class 536, subclass 23.1.

(Upon election of Group III, applicant must further choose one feature or a specific, defined combination of features from the Predictive Markers in Table 1 as each feature represents an independent invention, not a species)

It is noted for Applicant's convenience that this is a requirement for the election of a Group for examination NOT a requirement for an election of species because although the claims are presented in Markush format, the claims are drawn to methods using multiple agents which do not share, as a whole, a substantial structural feature disclosed as being essential to their utility. Thus, the

analysis of the claims, for restriction purposes, is subject to the findings of the court wherein the court found that unity of invention exists where entities included within a Markush group share a substantial structural feature disclosed as being essential to utility of the invention, In re Harnisch, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Since the members of the group do not share a substantial structural feature disclosed as being essential to utility of the invention, the group as claimed fails the Harnisch test and the claims are not accorded Markush restriction practice because they do not meet the requirements to be accorded Markush practice under MPEP 803.02.

The above inventions are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the patentability of the combination does not rely necessarily and solely on the patentability of any one subcombination and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the patentability of the combination does not rely necessarily and solely on the patentability of any one subcombination as clearly evidenced by the plural subcombinations claimed. Further, each of the subcombinations has utility by itself because each of the subcombinations is useful for screening for different variables and different markers. Thus the claims are distinct as required by MPEP 806.05(c).

IV. Claim 25, drawn to a kit for determining a bortezomib therapy for treating a tumor in a patient comprising reagents for assessing the expression of the predictive marker set of claim 1 and instructions for use, drawn to detecting proteins, classified in class 530, subclass 387.1.

(Upon election of Group IV, applicant must further choose one feature or a specific, defined combination of features from the Predictive Markers in Table 1 as each feature represents an independent invention, not a species)

It is noted for Applicant's convenience that this is a requirement for the election of a Group for examination NOT a requirement for an election of species because although the claims are presented in Markush format, the claims are drawn to methods using multiple agents which do not share, as a whole, a substantial structural feature disclosed as being essential to their utility. Thus, the analysis of the claims, for restriction purposes, is subject to the findings of the court wherein the court found that unity of invention exists where entities included within a Markush group share a substantial structural feature disclosed as being essential to utility of the invention, In re Harnisch, 631 F.2d 716, 206

USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Since the members of the group do not share a substantial structural feature disclosed as being essential to utility of the invention, the group as claimed fails the Harnisch test and the claims are not accorded Markush restriction practice because they do not meet the requirements to be accorded Markush practice under MPEP 803.02.

The above inventions are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the patentability of the combination does not rely necessarily and solely on the patentability of any one subcombination and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the patentability of the combination does not rely necessarily and solely on the patentability of any one subcombination as clearly evidenced by the plural subcombinations claimed. Further, each of the subcombinations has utility by itself because each of the subcombinations is useful for screening for different variables and different markers. Thus the claims are distinct as required by MPEP 806.05(c).

Claim 34 links inventions V and VI. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claim 34. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP ' 804.01.

V. Claims 35-39, drawn to a method for determining a proteasome inhibition therapy regimen for treating a tumor in a patient comprising: a) determining the level of expression of Predictive marker No. 149; and b) determining a proteasome inhibition-based regimen for treating the tumor based on the expression of the predictive marker, wherein a significant expression level is indicative that the

patient is either a responsive patient or a non-responsive patient, wherein the level of the expression of the feature in the predictive marker set is determined by detection of mRNA, classified in class 435, subclass 6.

VI. Claims 36-39, drawn to a method for determining a proteasome inhibition therapy regimen for treating a tumor in a patient comprising: a) determining the level of expression of Predictive marker No. 149; and b) determining a proteasome inhibition-based regimen for treating the tumor based on the expression of the predictive marker, wherein a significant expression level is indicative that the patient is either a responsive patient or a non-responsive patient, wherein the level of the expression of the feature in the predictive marker set is determined by detection of protein, classified in class 435, subclass 7.1.

Claim 40 links inventions VII and VIII. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claim 40. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP ' 804.01.

VII. Claim 41, drawn to a kit for determining a proteasome inhibition therapy for treating a tumor in a patient comprising reagents for assessing the expression of

Predictive Marker No. 149, and instructions for use, drawn to detecting nucleic acids classified in class 536, subclass 23.1.

VIII. Claim 40, drawn to a kit for determining a proteasome inhibition therapy for treating a tumor in a patient comprising reagents for assessing the expression of Predictive Marker No. 149, and instructions for use, drawn to detecting proteins, classified in class 530, subclass 387.1.

The inventions are distinct, each from the other because of the following reasons:

1. Inventions of Groups I, II, V, and VI are directed to related methods. The related inventions are distinct if the (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; (2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP § 806.05(j).

In the instant case, the inventions as claimed are distinct each from the other in that different designs and modes of operation and do not overlap in scope. For example the inventions of Group I and II are drawn to a method for determining a bortezomib therapy regimen for treating a liquid tumor in a patient, wherein the level of the expression of the feature in the predictive marker set is determined by detection of the distinct molecules mRNA or protein, respectively. Additionally, Groups V and VI drawn to a method for determining a proteasome inhibition therapy regimen for treating a tumor in a patient comprising: a) determining the level of expression of Predictive marker No. 149; and b) determining a proteasome inhibition-based regimen for treating the tumor based on the expression of the

predictive marker, wherein a significant expression level is indicative that the patient is either a responsive patient or a non-responsive patient, wherein the level of the expression of the feature in the predictive marker set is determined by detection of the distinct molecules mRNA or protein, respectively. Furthermore, the inventions as claimed do not encompass overlapping subject matter and there is nothing of record to show them to be obvious variants.

Furthermore, searching all of the inventions of Groups I, II, V, and VI would invoke a burdensome search. Some of the inventions have been classified separately. Thus, each of these inventions has attained recognition in the art as a separate subject for inventive effort, and also a separate field of search. Although some of the inventions are classified similarly, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not coextensive and is much more important in evaluating the burden of search.

2. Inventions of Group I and Group III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the nucleic acid probes could be used in the construction of vectors for expressing mRNA for protein production or as antisense inhibitors of mRNA.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the

inventions have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

3. Inventions of Groups IV, VII, and VIII and Group I are directed to unrelated products and process. Product and process inventions are unrelated if it can be shown that the product cannot be used in, or made by, the process. See MPEP § 802.01 and § 806.06. In the instant case, Groups IV and VIII are drawn to detecting proteins and Group I is a method drawn to the detection of mRNA, thus the products of Groups IV and VIII cannot be used in the method of Group I. Additionally, Group VII is drawn to a kit only for the detection of Predictive Marker No. 149 by detection of mRNA and Group I is drawn to the determining the levels of multiple Predictive Markers at the mRNA level, thus the product of Group VII cannot be used in the method of Group I.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

4 Inventions of Group II and Group IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that

product. See MPEP § 806.05(h). In the instant the kit for detecting proteins could be used for affinity purification of the proteins.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

5. Inventions of Groups III, VII, and VIII and Group II are directed to unrelated products and process. Product and process inventions are unrelated if it can be shown that the product cannot be used in, or made by, the process. See MPEP § 802.01 and § 806.06. In the instant case, Groups III and VII are drawn to detecting nucleic acids and Group II is a method drawn to the detection of proteins, thus the products of Groups III and VIII cannot be used in the method of Group II. Additionally, Group VIII is drawn to a kit only for the detection of Predictive Marker No. 149 by detection of protein and Group II is drawn to the determining the levels of multiple Predictive Markers at the protein level, thus the product of Group VIII cannot be used in the method of Group II.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

6. Inventions of Groups III, IV, VII and VIII are directed to related products. The related inventions are distinct if the (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; (2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP § 806.05(j).

In the instant case, the inventions as claimed are distinct each from the other in that they different designs and functions. For example, Group III and IV are drawn to a kit for determining a bortezomib therapy for treating a tumor in a patient comprising reagents for assessing the expression of the predictive marker set of claim 1 and instructions for use, drawn to detecting nucleic acids and proteins, respectively. Additionally, Groups VII and VIII are drawn to a kit for determining a proteasome inhibition therapy for treating a tumor in a patient comprising reagents for assessing the expression of Predictive Marker No. 149, and instructions for use, drawn to detecting nucleic acids and proteins respectively. Furthermore, the inventions as claimed do not encompass overlapping subject matter and there is nothing of record to show them to be obvious variants.

Furthermore, searching all of the inventions of Groups I-VI would invoke a burdensome search. Some of the inventions have been classified separately. Thus, each of these inventions has attained recognition in the art as a separate subject for inventive effort, and also a separate field of search. Although some of the inventions are classified similarly, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not coextensive and is much more important in evaluating the burden of search.

7. Inventions of Group III and Group V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the nucleic acid probes could be used in the construction of vectors for expressing mRNA for protein production or as antisense inhibitors of mRNA.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

8. Inventions of Group III and Group VI are directed to an unrelated product and process. Product and process inventions are unrelated if it can be shown that the product cannot be used in, or made by, the process. See MPEP § 802.01 and § 806.06. In the instant case, Groups III is drawn to a kit for determining a bortezomib therapy for treating a tumor in a patient comprising reagents for assessing the expression of the predictive marker set of claim 1 and instructions for use, drawn to detecting nucleic acids and Group VI is a method drawn to the detection of proteins, thus the product of Group III cannot be used in the method of Group VI.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the

inventions have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

9. Inventions of Group IV and Group VI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant the kit for detecting proteins could be used for affinity purification of the proteins.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

10. Inventions of Group IV and Group V are directed to an unrelated product and process. Product and process inventions are unrelated if it can be shown that the product cannot be used in, or made by, the process. See MPEP § 802.01 and § 806.06. In the instant case, Group IV is drawn to a kit for determining a bortezomib therapy for treating a tumor in a patient comprising reagents for assessing the expression of the predictive marker set of claim 1 and instructions for use, drawn to detecting proteins and Group V is a method drawn to the detection of nucleic acids, thus the product of Group IV cannot be used in the method of Group V.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

11. Inventions of Group V and Group VII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the nucleic acid probes could be used in the construction of vectors for expressing mRNA for protein production or as antisense inhibitors of mRNA.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

12. Inventions of Group V and Group VIII are directed to an unrelated product and process. Product and process inventions are unrelated if it can be shown that the product cannot be used in, or made by, the process. See MPEP § 802.01 and § 806.06. In the instant case, Group VIII is a kit drawn to detecting proteins and Group V is a method drawn to the detection of mRNA, thus the product of Group VIII cannot be used in the method of Group V.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

13. Inventions of Group VI and Group VIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant the kit for detecting proteins could be used for affinity purification of the proteins.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

14. Inventions of Group VI and Group VII are directed to an unrelated product and process. Product and process inventions are unrelated if it can be shown that the product cannot be used in, or made by, the process. See MPEP § 802.01 and § 806.06. In the instant case, Group VII is a kit drawn to detecting nucleic acids and Group VI is a method drawn to the detection of protein, thus the product of Group VII cannot be used in the method of Group VI.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

Because these inventions are distinct for the reasons given above and the search required for one group is not required for another group, restriction for examination purposes as indicated is proper.

Species Elections for Groups I and II

A. Claim 1 is generic to the following patentably distinct species of criteria for selecting features in the predictive marker set as disclosed and contemplated:

1) having a rank under 100

2) having a rank over 100

2) having a rank of 100

B. Claim 1 is generic to the following disclosed patentably distinct species of "liquid tumor":

1) myelomas

2) multiple myloma

3) Non-Hodgkins Lympoma

4) B-cell lymphoma

5) Waldenstrom's syndrome

6) chronic lymphocytic leukemia

7) other leukemias

C. Claim 1 is generic to the following disclosed patentably distinct species of time for selecting the patient sample:

1) prior to tumor therapy

2) concurrently with tumor therapy

3) after tumor therapy

D. Claim 1 is generic to the following disclosed patentably distinct species of selection methods:

1) Signal-to-Noise Ratio method

2) Class-Based Threshold method

E. Claim 1 is generic to the following disclosed patentably distinct species of predictive marker sets selected by the method of claim 1:

1) Table 4

2) Table 5

3) Table 6

Species Elections for Groups V and VI

Claim 34 is generic to the following disclosed patentably distinct species of proteasome inhibitor for tumor treatment as contemplated and claimed:

1) bortezomib

2) peptidyl aldehyde

3) peptidyl boronic acid

4) peptidyl boronic ester

5) vinyl sulfone

6) epoxyketone

7) lactacystin analog

B. Claim 34 is generic is generic to the following disclosed patentably distinct species of tumor:

1) liquid

2) solid

If applicant elects species B-1, liquid tumor, then applicant must elect from species group C.

C. Claim 34 is generic to the following disclosed patentably distinct species of liquid tumor:

1) myelomas

2) multiple myloma

3) Non-Hodgkins Lympoma

4) B-cell lymphoma

5) Waldenstrom's syndrome

6) chronic lymphocytic leukemia

7) other leukemias

In accordance with the decisions in *In re Harnisch*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984), restriction of a Markush group is proper where the compounds within the group either (1) do not share a common utility, or (2) do not share a substantial structural feature disclosed as being essential to that utility. In addition, a Markush group may encompass a plurality of independent and distinct inventions where two or more members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the other member(s) obvious under 35 USC 103. Since the decisions in *In re Weber*, 198 USPQ 328 (CCPA 1978) and *In re Hass*, 198 USPQ 334 (CCPA 1978), it is proper for the Office to refuse to examine that which applicants regard as their invention, if the subject matter in a claim lacks unity of invention, see MPEP 803.02.

The above species are independent or distinct because they comprise structurally distinct molecules and have different modes of operation and different effects. Further, each species would require different searches and the consideration of different patentability issues.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species from each species group above for the elected invention Group, even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to

be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103 of the other invention.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be

amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Applicant is advised that the reply to this restriction requirement to be complete must include an election of the invention to be examined even though the requirement is traversed (37 CFR 1.143).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Peter J. Reddig, Ph.D.
Examiner
Art Unit 1642

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

PJR